

Appendix 5. Overview of RCT results of medical treatment of PAD

IMPROVING LEG SYMPTOMS		
Treatment	Effect	Level of Evidence
Smoking cessation	<ul style="list-style-type: none"> • May reduce claudication severity • May reduce risk of developing rest pain 	Level III†
Exercise	<ul style="list-style-type: none"> • Significantly improves maximal walking time and walking ability • More effective than angioplasty or antiplatelet therapy • Similar efficacy to surgical revascularization 	Level I
Statins	<ul style="list-style-type: none"> • Significantly reduce incidence of new intermittent claudication • Improve pain-free walking time 	Level I
Blood pressure lowering medications	<ul style="list-style-type: none"> • ACEI help improve leg symptoms • Beta-blockers do not worsen but do not help leg symptoms 	Level I-2
Cilostazol (Pletal)	<ul style="list-style-type: none"> • Improves claudication symptoms at 12–24 weeks offset by side effects (headache, diarrhea, palpitations) 	Level I
Antiplatelet therapy - aspirin/ASA - clopidogrel (Plavix®) - ticlopidine* (Ticlid®)	<ul style="list-style-type: none"> • Significantly reduces risk of arterial occlusion • Delays progression and reduces need for intervention • Reduces graft failure • Ticlopidine shown to significantly increase pain-free walking distance, but ASA not shown to improve claudication symptoms 	Level I
Ginkgo biloba special extract (Egb 761)	<ul style="list-style-type: none"> • Significantly increases pain-free walking distance 	Level I-2
Pentoxifylline, testosterone, levocarnitine	<ul style="list-style-type: none"> • Efficacy either not demonstrated or less effective than established treatment 	Not proven
Growth factors and autologous bone marrow cells	<ul style="list-style-type: none"> • Under investigation 	No data
Anticoagulants	Heparin, low-molecular-weight heparin, oral anticoagulants	No benefit
PREVENTING SYSTEMIC CARDIOVASCULAR COMPLICATIONS		
Treatment	Effect	Level of Evidence
Smoking cessation	<ul style="list-style-type: none"> • No RCTs but convincing observational data in PAD • Rapid reduction in cardiovascular risk in general population 	Level II-2†
Blood pressure lowering medications	<ul style="list-style-type: none"> • Magnitude of benefit associated with magnitude of blood pressure lowering • Uncertain whether: <ul style="list-style-type: none"> • ACE inhibitors and angiotensin II receptor antagonists have significant additional effects • Beta-blockers are less effective 	Level I
Statins	<ul style="list-style-type: none"> • Significantly reduce risk of stroke, MI, vascular death and revascularization 	Level I
Antiplatelet therapy - aspirin/ASA - clopidogrel - ticlopidine* - picotamide, triflusal, ketanserin	<ul style="list-style-type: none"> • Results of meta-analyses with antiplatelet therapy in PAD are consistent • Among high-risk patients, including those with PAD, significantly reduces risk of MI, stroke, cardiovascular death by about 25% • Clopidogrel significantly reduces relative risk of MI, stroke, or cardiovascular death compared with aspirin; more expensive than ASA • Ticlopidine reduces risk of MI, stroke, or death by approximately one-third in patients with PAD • Novel antiplatelet agents have not demonstrated superiority to aspirin or clopidogrel 	Level I novel agents not proven
Weight loss	<ul style="list-style-type: none"> • Observational data indicate increasing waist-hip ratio and BMI increase cardiovascular risk • No RCT evidence yet that weight loss affects vascular events 	Uncertain benefit
Glycemic control	<ul style="list-style-type: none"> • No significant effect on stroke, MI, death, or amputation due to PAD, although intensive control reduces microvascular diabetic complications 	No proven benefit

† Randomized controlled trials unethical in patients who smoke

* Due to the potential for thrombocytopenia, thrombocytopenic purpura and potentially fatal neutropenia, ticlopidine has largely been replaced by clopidogrel

Adapted from: (1) Hankey GJ, Norman PE, Eikelboom JW. Medical treatment of peripheral arterial disease. *JAMA* 2006; 295(5):547-553; (2) Cassar K, Bachoo P. Peripheral arterial disease. *BMJ Clinical Evidence* 2004.

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